

IN THE CLAIMS:

Please substitute the following claims for the previous claims.

1. (previously presented) A particulate composition for delivery to the pulmonary system, the composition comprising:
particles comprising an active agent, a saturated phospholipid and a polyvalent cation, wherein the molar ratio of polyvalent cation to phospholipid is at least 0.05 and is sufficiently high to increase the gel-to-liquid crystal transition temperature of the particles compared to particles without the polyvalent cation.
2. (original) A particulate composition according to claim 1 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 20°C.
3. (original) A particulate composition according to claim 2 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 40°C.
4. (original) A particulate composition according to claim 1 further comprising a surfactant selected from the group consisting of nonionic detergents, nonionic block copolymers, ionic surfactants and combinations thereof.
5. (original) A particulate composition according to claim 4 wherein the surfactant is selected from the group consisting of sorbitan esters, ethoxylated sorbitan esters, fatty acids, salts, sugar esters, ethylene oxides, and combinations thereof.
- 6-7. (cancelled)
8. (original) A particulate composition according to claim 1 wherein the polyvalent cation is a divalent cation.

9. (previously presented) A particulate composition according to claim 8 wherein the divalent cation is selected from the group consisting of calcium, magnesium and zinc.

10. (cancelled)

11. (previously presented) A particulate composition according to claim 8 wherein the molar ratio of divalent cation to phospholipid is 0.05 – 2.0.

12. (previously presented) A particulate composition according to claim 8 wherein the molar ratio of divalent cation to phospholipid is 0.25 – 1.0.

13. (original) A particulate composition according to claim 12 wherein the divalent cation is calcium.

14. (previously presented) A particulate composition according to claim 13 wherein the molar ratio of calcium to phospholipid is about 0.50.

15. (original) A particulate composition according to claim 1 wherein the phospholipid comprises a natural or synthetic lung surfactant.

16. (cancelled)

17. (previously presented) A particulate composition according to claim 1 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

18. (previously presented) A particulate composition according to claim 1 further comprising a polymer selected from the group consisting of polysaccharides, polyvinyl alcohol, polyvinyl pyrrolidone, polylactides, polyglycolides, polyethylene glycol, and mixtures thereof.

19. (original) A particulate composition according to claim 1 comprising particles having a mass median diameter of less than 20 microns.

20. (original) A particulate composition according to claim 19 wherein the mass median diameter is within 0.5 – 5 microns.

21. (original) A particulate composition according to claim 19 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

22. (original) A particulate composition according to claim 21 wherein the aerodynamic diameter is within 0.5 – 5 microns.

23. (original) A particulate composition according to claim 1 comprising an emitted dose of at least 40%.

24. (original) A particulate composition according to claim 1 comprising an emitted dose of at least 60%.

25. (original) A particulate composition according to claim 1 comprising an emitted dose of at least 90%.

26. (original) A particulate composition according to claim 1 further comprising a non-aqueous suspension medium.

27. (original) A particulate composition according to claim 1 further comprising an excipient selected from the group consisting of amino acids, carbohydrates, inorganic salts, organic salts, carboxylic acids, and mixtures thereof.

28. (original) A particulate composition according to claim 27 wherein the excipient is selected from the group consisting of hydrophobic amino acids, monosaccharides, disaccharides, polysaccharides, sodium citrate, citric acid, ammonium carbonate, ammonium acetate, and ammonium chloride.

29. (previously presented) A particulate composition according to claim 1 wherein the bulk density of the particulate composition is less than 0.5 g/cm^3 .

30. (previously presented) A particulate composition according to claim 29 wherein the bulk density of the particulate composition is less than 0.05 g/cm^3 .

31. (previously presented) A particulate composition comprising:
particles comprising an active agent, a saturated phospholipid and a polyvalent cation, wherein the molar ratio of polyvalent cation to phospholipid is at least 0.05 and wherein the composition has a gel-to-liquid transition temperature at least 20°C higher than room temperature.

32. (previously presented) A particulate composition for delivery to the pulmonary system, the composition comprising porous particles comprising:
20 – 99.9% of a saturated phospholipid;
a polyvalent cation; and
0.1 – 80% active agent;
wherein the molar ratio of polyvalent cation to phospholipid is at least 0.05.

33-43. (cancelled)

44. (previously presented) A method of delivering an active agent to a patient in need thereof, the method comprising:

administering to the respiratory tract of the patient an effective amount of particles comprising an active agent, a saturated phospholipid and a polyvalent cation, wherein the molar ratio of polyvalent cation to phospholipid is at least 0.05 and is sufficiently high to increase the gel-to-liquid crystal transition temperature of the particles compared to particles without the polyvalent cation.

45. (original) A method according to claim 44 wherein the particulate composition comprises particles having a mass median diameter of less than 20 microns.

46. (original) A method according to claim 45 wherein the mass median diameter is within 0.5 – 5 microns.

47. (original) A method according to claim 45 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

48. (original) A method according to claim 47 wherein the aerodynamic diameter is within 0.5 – 5 microns.

49. (currently amended) A method according to claim 44 wherein the particles comprise polyvalent cation at a molar ratio of polyvalent cation:phospholipid of 0.25-1.0.

50. (original) A method according to claim 49 wherein the polyvalent cation comprises calcium.

51. (previously presented) A method according to claim 48 wherein the particles comprise a bulk density of less than 0.5 g/cm³.

52. (previously presented) A method according to claim 51 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

53. (original) A particulate composition according to claim 1 wherein the particles are hollow and porous.

54. (previously presented) A particulate composition according to claim 1 comprising 0.1 – 80% w/w of the active agent.

55. (original) A particulate composition according to claim 31 wherein the particles are hollow and porous.

56. (cancelled)

57. (previously presented) A particulate composition according to claim 31 wherein the gel-to-liquid transition temperature is at least 40°C higher than room temperature.

58. (previously presented) A particulate composition according to claim 31 wherein the phospholipid is selected from dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

59. (previously presented) A particulate composition comprising:
particles comprising a structural matrix comprising a saturated phospholipid and a polyvalent cation, wherein the molar ratio of polyvalent cation to phospholipid is at least 0.05 and is sufficiently high to increase the gel-to-liquid crystal transition temperature of the particles compared to particles without the polyvalent cation, wherein the particles further comprise an active agent.

60. (original) A particulate composition according to claim 59 wherein the phospholipid comprises dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

61. (original) A particulate composition according to claim 59 wherein the polyvalent cation is a divalent cation.

62. (previously presented) A particulate composition according to claim 61 wherein the divalent cation is selected from the group consisting of calcium, magnesium, and zinc.

63. (cancelled)

64. (previously presented) A particulate composition according to claim 59 wherein the molar ratio of polyvalent cation to phospholipid is 0.05 – 2.0.

65. (previously presented) A particulate composition according to claim 59 wherein the molar ratio of polyvalent cation to phospholipid is 0.25 – 1.0.

66. (cancelled)

67. (previously presented) A particulate composition according to claim 59 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

68. (original) A particulate composition according to claim 61 wherein the divalent cation is calcium.

69. (original) A particulate composition according to claim 68 wherein the molar ratio of calcium to phospholipid is about 0.50.

70. (previously presented) A particulate composition according to claim 59 wherein the composition has a gel-to-liquid crystal transition temperature at least 20°C higher than room temperature.

71. (previously presented) A particulate composition according to claim 59 wherein the composition has a gel-to-liquid crystal transition temperature at least 40°C higher than room temperature.

72. (original) A particulate composition according to claim 1 wherein the saturated phospholipid is a saturated, zwitterionic phospholipid.

73. (original) A particulate composition according to claim 31 wherein the saturated phospholipid is a zwitterionic phospholipid.

74. (original) A particulate composition according to claim 32 wherein the saturated phospholipid is a zwitterionic phospholipid.

75. (original) A particulate composition according to claim 32 wherein the molar ratio of polyvalent cation to phospholipid is effective to increase the gel to liquid crystal transition temperature of the particles compared to particles without the polyvalent cation.

76. (original) A particulate composition according to claim 32 wherein the particles are hollow.

77. (original) A method according to claim 44 wherein the saturated phospholipid is a saturated zwitterionic phospholipid.

78. (original) A particulate composition according to claim 59 wherein the saturated phospholipid is a saturated, zwitterionic phospholipid.